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L3: Entry 1 of 98 File: USPT Mar 12, 2002

DOCUMENT-IDENTIFIER: US 6355677 B1
TITLE: Adrenoleukodystrophy treatments and drug screening

Brief Summary Paragraph Right (4):
The gene for X-ALD, identified by positional cloning, encodes a peroxisomal membrane protein (ALDP) with a predicted molecular mass of 83 kDa. Based on sequence homology, it belongs to the ATP-binding cassette (ABC) superfamily of transmembrane transporters, with the structure of a half-transporter. Although peroxisomal VLCF-acyl CoA synthetase activity is impaired in X-ALD, mutational analysis- and complementation studies.sup.20,21 have shown that the gene for ALDP and not that for VLCF-acyl CoA synthetase is responsible for X-ALD.

Brief Summary Paragraph Right (12):
According to another embodiment of the invention, a method is provided for treating a patient with adrenoleukodystrophy. An effective amount of an agent which increases the activity of a peroxisomal ATP binding cassette transmembrane transprter protein in the central nervous system of the patient is administered to the patient with adrenoleukodystrophy. As a result, the level of C24:0 or C26:0 fatty acids in the central nervous system of the patient is reduced.

Detailed Description Paragraph Right (6):
Any agent which increases the activity of a peroxisomal ATP binding cassette transmembrane transporter proteins can be used. These include both classical pharmacological agents as well as DNA molecules which encode such proteins. It has been found that ALDRP can functionally complement mutant ALDP found in adrenoleukodystrophy. Thus augmenting the number of DNA molecules in a cell which make such complementing proteins or augmenting the activity of the endogenous genes can have a beneficial effect on the patient. PMP70 and PMP69 may also be used to functionally complement mutant ALDP.

Detailed Description Paragraph Type 0 (21):
21. Braiterman, L. T. et al. Suppression of peroxisomal membrane protein defects by peroxisomal ATP binding cassette (ABC) proteins. Hum Mol Genet 7 239-247 (1998).

CLAIMS:

9. A method of treating a patient with adrenoleukodystrophy, comprising the step of:

administering to a patient with adrenoleukodystrophy an effective amount of an agent selected from 4-phenylbutyrate, phenylacetate and mixtures thereof which increases the activity of a peroxisomal ATP binding cassette transmembrane transporter protein ALDRP in the central nervous system of the patient, whereby the level of C24:0 or C26:0 fatty acids in the central nervous system of the patient is reduced.

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L4: Entry 1 of 73 File: USPT Mar 12, 2002

DOCUMENT-IDENTIFIER: US 6355677 B1
TITLE: Adrenoleukodystrophy treatments and drug screening

Detailed Description Paragraph Type 0 (23):
23. Holzinger, A., Kammerer, S., Berger, J. & Roscher. A. A. cDNA cloning and mRNA expression of the human adrenoleukodystrophy related protein (ALDRP), a peroxisomal ABC transporter. Biochem Biophys Res Commun 239, 261-264 (1997).

Detailed Description Paragraph Type 0 (26):
26. Shani, N., Jimenez-Sanchez, G. Steel. G., Dean. M. & Valle. D. Identification of a fourth half ABC transporter in the human peroxisomal membrane.Hum Mol Genet 6, 1925-1931 (1997).

Detailed Description Paragraph Type 0 (27):
27. Holzinger, A., Kammerer, S. & Roscher. A. A. Primary structure of human PMP69, a putative peroxisomal ABC-transporter. Biochem Biophys Res Commun 237, 152-157 (1997).

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L5: Entry 2 of 7 File: USPT Oct 9, 2001

DOCUMENT-IDENTIFIER: US 6300094 B1
TITLE: Polynucleotides encoding a novel ABC transporter

Brief Summary Paragraph Right (9):
In another particularly preferred embodiment of the invention, there is a novel Novel ABC transporter protein from Staphylococcus aureus comprising the amino acid sequence of Table 1 [SEQ ID NO:2], or a variant thereof

Brief Summary Paragraph Right (71):
In addition, a diagnostic assay in accordance with the invention for detecting over-expression of Novel ABC transporter protein compared to normal control tissue samples may be used to detect the presence of an infection, for example. Assay techniques that can be used to determine levels of a Novel ABC transporter protein, in a sample derived from a host are well-known to those of skill in the art. Such assay methods include radioimmunoassays, competitive-binding assays, Western Blot analysis and ELISA assays.

Brief Summary Paragraph Right (89):
The invention also provides the use of the polypeptide, polynucleotide or inhibitor of the invention to interfere with the initial physical interaction between a pathogen and mammalian host responsible for sequelae of infection. In particular the molecules of the invention may be used: in the prevention of adhesion of bacteria, in particular gram positive bacteria, to mammalian extracellular matrix proteins on in-dwelling devices or to extracellular matrix proteins in wounds; to block Novel ABC transporter protein-mediated mammalian cell invasion by, for example, initiating phosphorylation of mammalian tyrosine kinases (Rosenshine et al., Infect. Immun. 60:2211 (1992); to block bacterial adhesion between mammalian extracellular matrix proteins and bacterial Novel ABC transporter proteins that mediate tissue damage and; to block the normal progression of pathogenesis in infections initiated other than by the implantation of in-dwelling devices or by other surgical techniques.

Brief Summary Paragraph Right (93):
A further aspect of the invention relates to an immunological composition which, when introduced into an individual capable or having induced within it an immunological response, induces an immunological response in such individual to a Novel ABC transporter or protein coded therefrom, wherein the composition comprises a recombinant Novel ABC transporter or protein coded therefrom comprising DNA which codes for and expresses an antigen of said Novel ABC transporter or protein coded therefrom. The immunological response may be used therapeutically or prophylactically and may take the form of antibody immunity or cellular immunity such as that arising from CTL or CD4+T cells.

Brief Summary Paragraph Right (99):
While the invention has been described with reference to certain Novel ABC transporter protein, it is to be understood that this covers fragments of the naturally occurring protein and similar proteins with additions, deletions or substitutions which do not substantially affect the immunogenic properties of the recombinant protein.

L5: Entry 4 of 7 File: USPT Dec 19, 2000

DOCUMENT-IDENTIFIER: US 6162616 A
TITLE: Multidrug resistance-associated polypeptide

Brief Summary Paragraph Right (5):
A significant survival advantage is associated with the acquisition of a multidrug-resistance phenotype, which arises from expression of a cellular gene encoding a protein that removes diverse chemotherapeutic drugs or drug metabolites from the intracellular milieu. Drug export diminishes cytotoxic effect, thereby protecting the transformed cell from otherwise lethal chemotherapeutic drugs or drug concentrations. To date, two genes encoding multidrug-resistance export proteins have been identified in the human genome. The first of these, MDR1, encodes P-glycoprotein, a 170 kDa multispanning transmembrane protein belonging the ATP Binding Cassette (ABC) Transporter protein superfamily. Lautier et al. (1996), 52 Biochem. Pharmacol. 967-977. Superfamily members are multispanning transmembrane proteins that transport substances into or out of the intracellular environment in an energy-dependent manner. Higgins (1992), 8 Ann. Rev. Cell Biol. 67-113, provides a general overview of the properties and natural occurrence of superfamily member proteins. ABC transporters have been identified for a large variety of structurally diverse transported substrates, including sugars, peptides, inorganic ions, amino acids, polysaccharides and proteins. Individual transporter proteins appear to function unidirectionally, i.e., to carry out either export or import of intracellular substances. Thus, P-glycoprotein functions by exporting chemotherapeutic drugs which, although structurally heterogenous, appear to share hydrophobic properties. P-glycoprotein overexpression correlates with the presence of a multidrug-resistance phenotype in diverse tumor cell isolates and tumorigenic cell lines. Significant effort has been invested in the development of agents to block or attenuate P-glycoprotein mediated drug export. Such agents are referred to commonly as "chemosensitizers" or "MDR reversal agents," and are disclosed in Hait et al. (1992), U.S. Pat. No. 5,104,858; Sunkara et al. (1993), U.S. Pat. No. 5,182,293; Sunkara et al. (1993), U.S. Pat. No. 5,190,957; Ramu et al. (1993), U.S. Pat. No. 5,190,946; Powell et al. (1995), U.S. Pat. No. 5,387,685; Piwnica-Worms (1995), U.S. Pat. No. 5,403,574; Sarkadi et al. (1995), PCT Publication WO 95/31474; Sunkara et al. (1996), U.S. Pat. No. 5,523,304; Zelle et al. (1996), U.S. Pat. No. 5,543,423; Engel et al. (1996), U.S. Pat. No. 5,556,856; Powell et al. (1996), U.S. Pat. No. 5,550,149 and Powell et al. (1996), U.S. Pat. No. 5,561,141. However, P-glycoprotein overexpression does not account for all instances of the acquisition of a multidrug resistance phenotype. Lautier et al. (1996), 52 Biochem. Pharmacol. 967-977.

Brief Summary Paragraph Right (6):
A second multidrug-resistance gene identified to date in the human genome encodes multidrug-resistance associated protein (MRP), a 190 kDa multispanning transmembrane protein also belonging to the ABC Transporter protein superfamily. MRP is described in Deeley et al. (1996), U.S. Pat. No. 5,489,519, the teachings of which are incorporated by reference herein. MRP shares only 15% sequence identity with P-glycoprotein at the amino acid level. In addition, MRP differs from P-glycoprotein in its ability to expel specific types of chemotherapeutic drugs from the intracellular milieu. These differences are thought to arise from differences in the drug expulsion mechanism of the two proteins: MRP appears to act on a glutathione-derivatized drug metabolite, whereas P-glycoprotein appears to act on an underivatized drug. Lautier et al, (1996), 52 Biochem. Pharmacol. 967-977. Significantly, agents that block or interfere with P-glycoprotein function appear to have little crossreactivity with MRP. Thus, significant effort is being invested in

the development of substances (MDR reversal agents) that block or inhibit MRP function.

Brief Summary Paragraph Right (9):
The present invention capitalizes on the unexpected discovery of a novel gene encoding a hitherto-unknown multidrug-resistance associated polypeptide (MRP). This novel polypeptide, designated herein as MRP-.beta., is encoded in the human genome and is expected to be found in the genomes of additional mammals. MRP-.beta. likely is a transmembrane-spanning, energy-dependent transporter or pump, as are other members of the ATP Binding Cassette (ABC) Transporter Protein superfamily to which the known proteins MRP and P-glycoprotein belong. It is likely that MRP-.beta. is disposed in the plasma membrane of a mammalian cell, and functions by ejecting intracellular substances, such as chemotherapeutic drugs. Alternatively, MRP-.beta. may span a vesicular membrane, and function by sequestering intracellular substances. Elevated levels of expression of the novel MRP-.beta. gene, or of bioactivity of the novel MRP-.beta. polypeptide encoded by this gene, accordingly are expected to contribute to the emergence and/or persistence of a multidrug-resistance phenotype in transformed mammalian cells, such as carcinoma cells, including adenocarcinoma cells. Elevated expression or bioactivity of MRP-.beta. similarly is expected to contribute to the occurrence of a multidrug-resistance phenotype in sarcoma cells and in transformed cells of the hematopoietic lineage, including leukemias, lymphomas and lymphosarcomas. MRP-.beta. is likely to account for multidrug-resistant mammalian cell phenotypes that are refractory to treatment with reversal agents that interfere with expression, production and/or function of P-glycoprotein or of MRP.

Brief Summary Paragraph Right (15):
In a second aspect, the invention features an MRP-.beta. polypeptide, the amino acid sequence of which comprises SEQ ID No: 2. More generally, the invention provides MRP-.beta. polypeptides, and unique fragments (epitopes) thereof, that are encoded by any of the above-described MRP-.beta. nucleic acids. For example, the invention provides MRP-.beta. polypeptides, the amino acid sequences of which comprise a sequence sharing at least 75% sequence similarity (as defined herein) with SEQ ID No: 2. Such MRP-.beta. polypeptides include naturally-occurring variants (e.g., polymorphic variants, phylogenetic counterparts of the presently disclosed human MRP-.beta., and/or naturally-occurring mutant variants, particularly mutants associated with the process of somatic cell transformation or tumorigenesis) and biosynthetic variants produced by routine molecular engineering techniques. Based upon an assessment of its sequence similarity to known proteins, such as MRP, the present novel MRP-.beta. polypeptide is believed to be a novel member of the ABC Transporter Protein superfamily. Thus, it is anticipated that MRP-.beta. polypeptides will be displayed on the surface of cells expressing an MRP-.beta. gene, such as multidrug resistant tumor cells or transfected host cells. Of course, it is also possible that MRP-.beta. will be incorporated into intracellular phospholipid membranes, such as vesicular membranes. Cellular production of MRP-.beta. is expected to contribute to the emergence and/or persistence of a multidrug-resistant phenotype in transformed mammalian cells. The present invention provides various specific MRP-.beta. polypeptide embodiments, including MRP-.beta. polypeptides immunogenically displayed on intact host cell membranes or cell-free membrane fractions derived from host cells; MRP-.beta. polypeptides incorporated into synthetic or non-cellular phospholipid membranes or micelles, and MRP-.beta. polypeptides and polypeptide fragments isolated in substantially pure form. Any of the foregoing polypeptides, or unique, immunogenic fragments (epitopes) thereof can be used to induce immune responses in human or nonhuman mammals.

Brief Summary Paragraph Right (17):
In a fourth aspect, the invention features expression vectors comprising nucleic acid encoding an MRP-.beta. polypeptide comprising an amino acid sequence that shares at least 75% sequence similarity with SEQ ID No: 2. The nucleic acid sequence of an exemplary expression vector thus comprises SEQ ID No: 1. The nucleic acid sequence of another exemplary expression vector comprises the sequence of MRP-.beta. cDNA deposited on even date herewith. Additional exemplary expression vectors comprise nucleic acid encoding variants, whether biosynthetic or naturally-sourced, of the presently disclosed MRP-.beta. polypeptide. Certain embodiments of the present expression vectors encode chimeric polypeptides in which one or more

MRP-.beta. amino acid residues are substituted by the corresponding residues of another ABC Transporter Protein superfamily member, such as MRP or P-glycoprotein. Such embodiments are expected to facilitate elucidation of the molecular basis of multidrug resistance phenotypes, and thence to facilitate design or screening of novel inhibitors of multidrug resistance. In addition to nucleic acid encoding the MRP-.beta. polypeptide, the present expression vectors comprise one or more expression control elements (e.g., promoter, transcriptional initiation site, termination site and the like) to direct the production of the encoded MRP-.beta. polypeptide in prokaryotic or, preferably eukaryotic, host cells. Optionally, the present expression vectors further comprise a selectable marker gene. For use with eukaryotic host cells, the present expression vector may still further comprise one or more retroviral components to promote infectivity and uptake by eukaryotic, preferably mammalian, cells.

Brief Summary Paragraph Right (27):
Further general aspects of the invention feature therapeutic methods and compositions, including one or more modulators (stimulators or, preferably, inhibitors) of the expressed MRP-.beta. gene and/or protein. Accordingly, the invention provides means for mitigating (detectably decreasing or otherwise affecting) aberrant expression of an MRP-.beta. gene, or aberrant production or biological function of an MRP-.beta. polypeptide. The invention thus provides means for attenuating an undesirable phenotype, such as a disease-associated phenotype, that is contributed to by MRP-.beta.. In preferred embodiments, the invention provides means for attenuating a multidrug-resistance phenotype, particularly a phenotype contributed to by MRP-.beta.. More particularly, a seventh aspect of the invention features methods for mitigating aberrant expression of an MRP-.beta. gene, and/or aberrant alteration or biological function of an MRP-.beta. polypeptide. One embodiment involves the administration of an antisense pharmaceutical composition of the present invention to a mammal suffering from effects of the aberrant phenotype associated with altered expression and/or function of MRP-.beta.. Another embodiment involves the administration of an antibody or fusion polypeptide of the present invention. In either embodiment, the therapeutic agent is administered systemically or locally under conditions sufficient to mitigate or attenuate the aberrant MRP-.beta. associated phenotype. Preferably, the therapeutic agent is administered under conditions sufficient to destroy cells aberrantly producing MRP-.beta.. In this manner, the invention provides means for destroying multidrug-resistant tumor cells in situ in the body of a mammal. In preferred embodiments, either of the foregoing therapeutic agents can be administered as an adjuvant to conventional chemotherapy. That is, either of the foregoing therapeutic agents can be coadministered together with one or more chemotherapeutic drugs. The present antisense or fusion polypeptide therapeutic agent can be administered prior to, concomitant with, or following administration of one or more chemotherapeutic drugs. In such embodiments, the antisense pharmaceutical composition mitigates resistance of MRP-.beta. expressing cells to the cytotoxic effects of the chemotherapeutic drug. That is, the antisense composition attenuates the MRP-.beta. phenotype, which is expected to be characterized by display of an ABC Transporter Protein family member (MRP-.beta.) and by the property of multidrug resistance. This is accomplished by disrupting activation or transcription of the MRP-.beta. gene, or by destabilizing RNA transcripts thereof. Diminished or discontinued expression of MRP .beta renders cells more susceptible to the cytotoxic effects of a chemotherapeutic drug that otherwise would be exported by MRP-.beta.. Similarly, a therapeutically administered cytotoxic fusion polypeptide localizes in the vicinity of cells aberrantly displaying MRP-.beta., producing cytolysis thereof. A chemoattractant fusion polypeptide also localizes to MRP-.beta. displaying cells, stimulating destruction thereof by macrophages, killer T cells or cytotoxic T cells.

Drawing Description Paragraph Right (3):
FIGS. 2A-2B is a text representation comprising aligned amino acid sequences of the known ABC Transporter Protein superfamily member MRP (described in Deeley et al. (1996) U.S. Pat. No. 5,489,519), and of the novel MRP-.beta. disclosed herein. Dashes (-) indicate gaps introduced to maximize alignment of similar sequences; asterisks (*) indicate the locations of identical aligned amino acid residues.

Detailed Description Paragraph Right (2):

The functional property of multidrug-resistance is associated with expression and cell-surface display of one or more ABC Transporter Protein superfamily members with energy-dependent export function (e.g., P-glycoprotein, MRP or MRP-.beta. as disclosed herein). The cell population described in Mirski et al. (1987) was reported in Cole et al. (1992), 258 Science 1650-1654 to overexpress MRP (a correction of the reported MRP sequence appears at 260 Science 879). Currently, antibodies specifically reactive with P-glycoprotein or MRP, or nucleic acid probes specific for the corresponding expressed nucleic acid sequences, are used to ascertain the molecular basis of multidrug-resistance in a given cell population. Where the cell population in question includes transformed cells in the body of a cancer sufferer, determination of the molecular basis of the observed phenotype can assist the clinician in ascertaining whether treatment with one of the so-called "chemosensitizers" or "MDR reversal agents," the majority of which affect P-glycoprotein, is appropriate. Thus, knowledge of the molecular basis of the observed phenotype provides information relevant to developing or revising a course of disease management. Zaman et al. (1993), 53 Cancer Res. 1747-1750, cautions, however, that the induction or overexpression of MRP does not account for all forms of multidrug-resistance phenotype that are not attributable to P-glycoprotein expression. The discovery of MRP-.beta., reported herein, establishes that additional members of the ABC Transporter Protein family exist in the mammalian (e.g., human) genome and likely contribute to the occurrence of multidrug-resistance in transformed cells.

Detailed Description Paragraph Right (17):
The present host cells initially are expected to facilitate production of MRP-.beta. polypeptides and structural and functional analysis thereof. The MRP-.beta. polypeptide comprising SEQ ID No: 2 is expected to bind ATP, and to be an integral, multispanning transmembrane protein generally as described in Almquist et al. (1995), 55 Cancer Res. 102-110. A significant portion of the total MRP-.beta. produced in host cells is expected to span the cells' plasma membrane, with an additional portion being present intracellularly, e.g., in the endoplasmic reticulum and/or the Golgi apparatus. Thus, MRP-.beta. host cells are expected to display extracellular portions of the multispanning MRP-.beta. polypeptide on the cell surface, appropriately configured to mediate the ATP-dependent sequestration or export (efflux) of a plurality of cytotoxic drugs, including drugs conventionally used as chemotherapeutic agents. These general properties are deduced from an assessment of the primary structure (sequence) of the MRP-.beta. polypeptide. FIG. 2 sets forth an exemplary sequence alignment of the disclosed novel MRP-.beta. polypeptide (SEQ ID No: 2), with relevant sequence of the MRP polypeptide of Deeley et al. (1996), U.S. Pat. No. 5,489,519. The alignment and identity calculations were obtained through application of the well-known Smith-Waterman algorithm for local alignment, using the PAM 120 scoring matrix described in Altschul et al. (1990), 215 J. Mol. Biol. 403-410, which ascertains the best match between two or more sequences regardless of overall differences in sequence length. MRP-.beta. shares approximately 42.5% amino acid sequence identity with MRP over the maximally aligned 894 amino acid residues. MRP-.beta. accordingly is considered to be a novel member of the ABC Transporter Protein superfamily and is deemed likely to contribute to multidrug-resistance phenotypes by mediating drug transport across cellular phospholipid membranes.

Detailed Description Paragraph Right (27):
It will be appreciated that the causes of multidrug-resistance phenotypes vary with each individual cell type and are not wholly accounted for by expression or overexpression of P-glycoprotein, MRP or the novel MRP-.beta. disclosed herein. Rather, additional members of the ABC Transporter Protein family may be involved, as may be one or more members of known or novel signal tranduction pathways or intracellular metabolic or growth-regulatory pathways. The present discovery of MRP-.beta. facilitates investigation into the role(s) of such additional gene expression products in the acquisition and/or maintenance of a multidrug-resistance phenotype. Specifically, the discovery of MRP-.beta. provides an improved method of identifying a gene, especially a hitherto unknown gene, expression of which contributes to emergence or maintenance of drug-resistant phenotype in transformed mammalian cells.

Detailed Description Paragraph Right (32):

Abnormal or aberrant phenotypes, especially multidrug-resistance associated phenotypes, that are contributed to by abnormalities affecting MRP-.beta., can be treated using pharmaceutical or therapeutic compositions provided herein. More specifically, the invention provides therapeutic compositions, including prophylactic, palliative and remedial compositions, useful for treatment of any disease state or deleterious condition contributed to by an abnormality affecting MRP-.beta.. A first category of such therapeutic compositions comprise an antisense oligonucleotide, or a vector encoding an antisense oligonucleotide, that hybridizes to nucleic acid corresponding to or transcribed from a cellular MRP-.beta. gene. Stewart et al. (1996), 51 Biochem. Pharmacol. 461-469, and Baracchini et al. (1996), U.S. Pat. No. 5,510,239, report successful, antisense-mediated attenuation of an MRP multidrug-resistance phenotype in cultured H69AR cells: exposure to antisense oligonucleotides significantly reduced intracellular MRP transcript and polypeptide levels. The techniques and administration methods disclosed therein can be adapted to provide antisense-mediated attenuation of an MRP-.beta. phenotype as disclosed herein. Stewart et al. (1996) report, however, that attenuation was achieved only transiently, due to the rate of cellular production of new MRP gene transcripts and/or degradation of the antisense oligonucleotide. Stewart et al. (1996) notes that, in the adriamycin selected multidrug-resistant H69AR cells, the phenotype cannot be attributed entirely to MRP expression, and for this reason counsels that antisense oligonucleotides should be used that are complementary to gene regions known to be conserved among members of the ABC Transporter Protein family. Similarly, Smyth et al. (1996), PCT Publ. WO 96/02556, reports successful, antisense oligonucleotide mediated, attenuation of a P-glycoprotein based multidrug resistance phenotype in cultured cells wherein the phenotype arises solely from P-glycoprotein production. By their nature, antisense oligonucleotides are limited to disruption of their specific target genes. Thus, the desired result of phenotypic attenuation will not be achieved where the multidrug resistance phenotype arises from (or is preserved by) expression of one or more previously unknown genes, to which the antisense oligonucleotide is unable to hybridize effectively under intracellular conditions.

Detailed Description Paragraph Right (63):

Without being limited by speculation, it is likely that MRP-.beta. confers the above-described survival advantage by mediating sequestration or efflux of one or more cytotoxins. That is, it is likely that MRP-.beta. is a member of the ABC Transporter Protein superfamily that carries out an export function. However, routine empirical testing is required to confirm whether MRP-.beta. exports one or more toxic substances, or imports one or more nutrients or energy sources, such as sugars or fatty acids of dietary or other metabolic origin. A number of conventional protocols can be practiced, with such routine modifications as may be deemed appropriate by the practitioner, to establish whether MRP-.beta. mediates toxin export. A presently preferred technique capitalizes on the fluorescent properties of anthracycline toxins (including adriamycin (doxorubicin) and daunamycin), such that toxin accumulation and/or efflux from MRP-.beta. expressing host cells can be monitored by fluorescence histochemistry or, preferably, by fluorescence-activated flow cytometry. An example of this technique is described in Krishan (1990), 33 Meth. Cell Biol. 491-500, incorporated herein by reference.

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L5: Entry 7 of 7 File: USPT Oct 5, 1999

DOCUMENT-IDENTIFIER: US 5962320 A
TITLE: Engineered antigen presenting cells and methods for their use

CLAIMS:

1. A cell of heterologous or xenogeneic origin that is not a professional antigen presenting cell, wherein said cell is engineered to express at least one ABC transporter protein and at least one costimulation molecule to function as an antigen presenting cell.

10. A cell that is not a professional antigen presenting cell, wherein said cell is engineered to present a selected antigen to T cells and to suppress T cell activation by the selected antigen, and wherein said cell expresses at least one ABC transporter protein and at least one chemokine.

19. A cell line that is not a professional antigen presenting cell line, wherein said cell line is engineered to express human HLA class I and class II molecules of different antigen specificity than the endogenous HLA molecules of said cell line and at least one ABC transporter protein.

20. The cell line of claim 19, wherein said ABC transporter protein is selected from the group consisting of TAP-1 and TAP-2 proteins.